I. Scientific Abstract

This is a phase I trial to evaluate DNA vaccination in patients with relapsed prostate cancer. The objective of this study is to determine the safety and immunogenicity of vaccination with the genes coding for mouse and human prostate specific membrane antigen (PSMA) in patients who are HLA-A0201+. We will assess whether DNA vaccination is safe and generates an immune response to an otherwise poorly immunogenic prostate differentiation antigen.

Studies in animal models have demonstrated that xenogeneic DNA (i.e., homologous DNA from a different species) can be more potent in inducing antibody and T cell responses against melanoma differentiation antigens than vaccination with self DNA. The hypothesis that xenogeneic DNA encoding a homologous antigen is more potent than syngeneic DNA encoding a tumor antigen will be tested. This will be assessed using a randomized phase I crossover design with two closely related DNA vaccines against PSMA. Patients will be randomly assigned to vaccination with either xenogeneic (mouse) or human PSMA DNA delivered intramuscularly at three different dose levels (100, 500, or 1500 μg in divided doses) every three weeks for three immunizations. Following this initial vaccination period, those patients previously randomized to receive mouse PSMA DNA will receive three immunizations with human PSMA DNA at three week intervals. Likewise, those patients initially randomized to receive human PSMA DNA will then receive three immunizations with mouse PSMA DNA at three week intervals. If patients have stable or clinically responding disease, additional vaccinations can be administered bimonthly for up to four additional vaccinations. A total of at least 36 patients are planned. Patients' sera and peripheral blood mononuclear cells will be collected in order to measure the antibody and T cell responses induced by the vaccines. Specifically, titers of IgM and IgG antibodies against human and mouse PSMA will be measured for serological response and CD8+ T cells responses will be assessed by ELISPOT.